C. Remarks

The claims are 1-6 and 9, with claims 1, 2 and 9 being independent. Claims 1 and 2 have been amended for clarification. New claim 9 has been added. Support for the new claim may be found, inter alia, in the specification at page 12, lines 10-12, in the Examples and in the other claims. Reconsideration of the present claims is expressly requested.

Claims 1-6 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Mark Chee et al., "Accessing Generic Information with High-Density DNA Arrays," 274 Science 610-614 (1996) (Chee). The grounds of rejection are respectfully traversed.

Prior to addressing the merits of rejection, Applicants once again would like to briefly review some of the key features and advantages of the presently claimed invention, particularly to aid the Examiner's understanding of what is meant by "plural" template patterns.

In the present invention, a probe arrays is prepared. In this probe array, at least two single-stranded nucleic acid probes are arranged in isolated spots on the substrates (one probe per spot). Then, a fluorescence-labeled, single-stranded nucleic acid, which has a base sequence fully complementary to one of the probes arranged on the substrate, is reacted with the probe array such that the two complementary single-stranded acids form a double-stranded nucleic acid. The unreacted, labeled single-stranded nucleic acid is removed, and the fluorescent intensity of each spot is measured. As a result of the

measurement, a template pattern is obtained.[1] This procedure is repeated until each single-stranded nucleic acid probe has been reacted with a labeled single-stranded nucleic acid that corresponds thereto and a template pattern for each such product has been obtained.

Therefore, as a result, a number of template patterns have been obtained, which number corresponds to the number of probes in the array. Since the array contains at least two probes, at least two template patterns are produced. Since the word "plural" means "relating to, consisting of, or containing more than one", these at least two template patterns are merely referred to by Applicants as a "plurality". Applicants' use of the phrase "reference dictionary" in the last-filed Amendment was merely to explain the use of the plural template patterns obtained using specific, known labeled single-stranded nucleic acids for comparative and identification purposes later in the claimed method.

The identification of a target single-stranded nucleic acid is made using the template patterns obtained as described above. The target nucleic acid is reacted with the array such that it forms a double-stranded nucleic acid with its complementary probe. After unreacted target acid has been removed, a fluorescent intensity at each of the array is measured, resulting in a sample template pattern. This sample template pattern is then compared with the plurality of template patterns that have already been obtained using

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1/ Applicants note that this description is for the process specifically recited in claim 1 and, for the most part, in new claim 9. Claim 2 involves a more detailed analysis and preparation of an additional template pattern for each probe spot from the results of a reaction with the labeled single-stranded nucleic acid in order to identify specific mismatches. However, the concept of preparing plural template patterns for later use as a means of identifying an unknown target is the same in all of the present claims.

known single-stranded nucleic acids[2] in order to identify a template pattern, which is substantially identical to the sample pattern. Thereafter, the specific single-stranded nucleic acid used for the preparation of the identified template pattern is identified to be the target single-stranded nucleic acid.

Chee does not disclose or suggest the above method. Chee only teaches comparing a fluorescent pattern obtained using a mutant sample with a fluorescent pattern obtained using a standard sample.

The DNA chip in Chee is a 4L tilted array where a vast number of probes, designated to have one base mismatch for every base position of a standard sequence, are arranged. Then, a template pattern for a standard sequence is obtained. Then, a hybridization pattern with a sample nucleic acid is obtained, and this pattern is compared with the standard pattern to identify a single base mutation, i.e., when the pattern obtained with a sample is different from the standard pattern, the base change can be directly read from the different intensities of the probes having A, T, G or C at that corresponding site. Chee does not disclose or suggest obtaining a template pattern for each probe spot using a fluorescence-labeled complementary single-stranded nucleic acid for each such spot and then comparing a test sample to these already obtained template patterns to identify which one of these plural template patterns matches the test sample.

In fact, the 4L tilted method used in Chee cannot directly identify a mutation when two or more mutations are present in close proximity (see right hand column on p. 611 and the legend of Fig. 2). According to the present invention, however, a target

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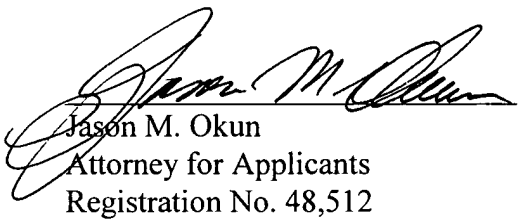
[2/] The "reference dictionary.

nucleic acid with mutations in close proximity to each other can be identified by comparing every possible template pattern (each obtained using known complementary single-stranded nucleic acids) with a sample pattern obtained with a target nucleic acid. In addition, in accordance with the present invention, template patterns may be obtained not only of one perfectly matched spot, but also for single mismatched spots, which can overcome the variation in fluorescent intensity resulting from various causes, thus leading to more reliable assay.

In conclusion, Applicants respectfully submit that it is clear that Chee does not disclose or suggest the presently claimed invention and cannot affect its patentability. Wherefore, it is respectfully requested that the outstanding rejection be withdrawn and the present case be passed to issue.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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